

METHACRYLATE PRODUCERS ASSOCIATION, INC.

1350 Eye Street, N.W., Suite 200, Washington, DC 20005

Office: (202) 962-9400 • Facsimile: (202) 289-3565

8EHQ-0697-13749

June 16, 1997

via messenger

Document Control Office (7407)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Room G-099
401 M Street, SW
Washington, DC 20460

PDW: 88860000229

Contains No CBI

97 JUN 16 AM 10:17

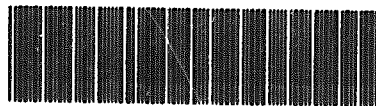
RECEIVED
OPT NCIC

Re: Supplement to Prior Notice in Accordance with TSCA Section 8(e)
Amended Final Report on Methacrylic Acid (MAA): (CAS No. 79-41-4)
TSCA 8(e) Document Control Number #8EHQ-0297-13749

Dear Sir/Madam:

On February 24, 1997, the Methacrylate Producers Association (MPA) submitted a final report for a DOT skin irritation test with methacrylic acid (CAS No. 79-41-4) in New Zealand Rabbits in accordance with TSCA Section 8(e). Enclosed is a copy of the amended final report for the study entitled "Methacrylic Acid: Skin Irritation Study in Rabbits." Please replace the previous report with this copy.

This submission is being made on behalf of the MPA member companies: CYRO Industries, Elf Atochem N.A., Inc., ICI Acrylics, Inc., and Rohm and Haas Company. If you have any questions about this submission, please contact me at (202) 962-9486.



8EHQ-96-13749

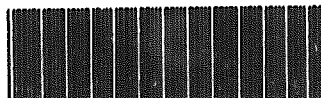
cc: MPA

Sincerely,

Elizabeth K. Hunt
Executive Director

97 JUN 18 AM 11:15

RECEIVED
OPT NCIC



89970000190

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132A

J.R. Parno

Revised Report Final: May 29, 1997

Applicable Guidelines:
OECD Guideline 404
US EPA 40 CFR Section 798.4470
EEC Directive 92/69/EEC B.4
U.S. D.O.T. Section 173.137

Rohm and Haas Company
Toxicology Department
727 Norristown Road
P. O. Box 904
Spring House, PA 19477-0904

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132A

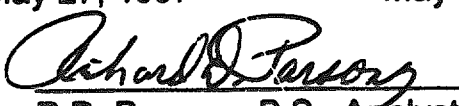
**THIS PAGE RESERVED FOR SPECIFIC
REGULATORY/COUNTRY REQUIREMENTS**

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132A

QUALITY ASSURANCE STATEMENT

This revised final report and the original raw data were reviewed for adherence to Good Laboratory Practices. This revised report is an accurate reflection of the raw data and an accurate description of the methods and standard operating procedures from this study. The following inspections were performed and reported to the Study Director and management:

	<u>Dates</u>	
<u>Inspections Performed</u>	<u>Inspected</u>	<u>Reported</u>
Dosing	July 23, 1996	September 18, 1996
Revised Draft Report	May 27, 1997	May 27, 1997
Revised Final Report	May 27, 1997	May 27, 1997


R.D. Parsons, B.S., Analyst 5/27/97
Quality Assurance Unit Date
Rohm and Haas Company

GLP COMPLIANCE STATEMENT


The study described in this revised final report was conducted in compliance with the following Good Laboratory Practice Standards except that chemical characterization of the test substance under a GLP Program was not conducted prior to the initiation of the study:

United States Environmental Protection Agency, Title 40 CFR Part 792, Toxic Substances Control act, published in the Federal Register, August 17, 1989;

Japan Ministry of Agriculture, Forests and Fisheries, 59 NohSan Notification No. 3850, Agricultural Production Bureau, August 10, 1984;

Organization for Economic Cooperation and Development, ISBN 92-64-12367-9, Paris 1992;


European Economic Community, Council Directive 87/18/EEC, December 18, 1986.


J.F. Pamo, M.S.
Study Director
Rohm and Haas Company

29-may-97
Date


J.E. McLaughlin, Ph.D.
Sponsor
Rohm and Haas Company

5/28/97
Date


H.E. Scribner, Ph.D., D.A.B.T.
Director of Toxicology
Rohm and Haas Company

5/28/97
Date

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132A



J.R. Parno, M.S.
Study Director
Rohm and Haas Company

29-may-97
Date

Revised Report Final: May 29, 1997

Rohm and Haas Company
Toxicology Department
727 Norristown Road
P. O. Box 904
Spring House, PA 19477-0904

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132A

KEY PERSONNEL PARTICIPATING IN THE STUDY

<u>Name</u> _____	<u>Responsibility</u>
J.R. Parno	Study Director
M.F. Lutz	Principal Investigator
L.P. Craig	Study Coordinator
K.B. Poorman	Animal Care Supervisor

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132A

ABSTRACT

Skin irritation of methacrylic acid (Lot No. 6/4/96, Toxicology Department Sample No. 96-054, 99.38% active ingredient) was assessed in New Zealand White rabbits. The undiluted test substance (0.5 ml) was applied topically to the shaved intact skin of one male rabbit. The application site was semi-occluded for 4 hrs. After the 4 hr exposure, the application site was wiped with paper towels saturated with tap water and blotted dry with paper towels. Skin irritation was evaluated according to Draize criteria at approximately 1, 24, 48, 72 hrs and at 7 and 14 days after patch removal. No mortality or clinical signs of systemic toxicity were observed during the study. Severe erythema and skin effects indicative of corrosivity (i.e., concave eschar) were observed. According to the Rohm and Haas Company Acute Toxicity and Irritation Hazard Categories (September, 1994), methacrylic acid is categorized as CORROSIVE to skin (i.e., evidence of irreversible destruction of dermal tissue).

Since corrosive findings were evident at 4 hrs, additional rabbits were tested to determine U.S. Department of Transportation (DOT) Packing Group classification. The undiluted test substance (0.5 ml) was applied topically to the shaved intact skin of one male rabbit on two separate sites for 1 hr (left side) and 3 minutes (right side). The 1 hr application site was semi-occluded with a fabric cuff and the 3 minute site was uncuffed during the exposure period. After each exposure period, the application sites were wiped with paper towels saturated with tap water and blotted dry with paper towels. Two additional rabbits received either a 1 hr or 3 minute exposure. A 1% soap solution was used on the additional rabbits exposed for the 1 hr or 3 minute period prior to the tap water rinse to assess whether more complete washing would prevent corrosivity. Skin irritation was evaluated according to Draize criteria at approximately 1, 24, 48, 72 hrs and at 7 and/or 14 days after patch removal. Severe erythema and skin effects indicative of corrosivity (i.e., concave eschar and erosion/ulceration) were observed on the 1 hr and 3 minute sites. According to United Nations (U.N.) and U.S. DOT Packing Group Classification guidelines for Class 8 materials (1993 and 1996, respectively), methacrylic acid is assigned to PACKING GROUP II (i.e., full thickness destruction at the site of contact on the intact skin of rabbits within 14 days after an exposure time of more than 3 minutes, but not more than 60 minutes).

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132A

TABLE OF CONTENTS

	<u>Page No.</u>
TITLE PAGE	1
RESERVED PAGE	2
QUALITY ASSURANCE STATEMENT	3
GLP COMPLIANCE STATEMENT	3
SIGNATURE PAGE	4
PERSONNEL PARTICIPATING IN THE STUDY	5
ABSTRACT	6
TABLE OF CONTENTS	7
 I. INTRODUCTION	 8
 II. MATERIALS AND METHODS	 8
A. Experimental Design	8
B. Test Substance	8
C. Animals and Animal Husbandry	8
D. Dose Preparation and Administration	9
E. Observations and Determinations	9
F. Location of Raw Data	10
 III. RESULTS	 10
 IV. CONCLUSIONS	 11
TABLE 1. Skin Irritation Scores (Draize Criteria) - 4 Hr	12
TABLE 2. Skin Irritation Scores (Draize Criteria) - 1 Hr	13
TABLE 3. Skin Irritation Scores (Draize Criteria) - 3 Minute	14
APPENDIX A. Skin Irritation Scoring (Draize Criteria)	15
APPENDIX B. United Nations and United States Department of Transportation Packing Group Classification Criteria	16
APPENDIX C. Changes to the Original Report (96R-132)	17

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132A

I. INTRODUCTION

This study was conducted to determine the skin irritation of methacrylic acid when applied to the shaved intact skin of rabbits. The study initiation (date protocol signed by Study Director) was July 18, 1996. The experimental start (day of dosing) and experimental termination (last day of observation) dates were July 23, 1996 and October 8, 1996, respectively.

II. MATERIALS AND METHODS

A. Experimental Design

<u>Test Substance</u>	<u>Exposure</u>	<u>Dose</u>	<u>No. of Rabbits</u>
methacrylic acid	4 hrs	0.5 ml	1
methacrylic acid	1 hr	0.5 ml	2
methacrylic acid	3 min.	0.5 ml	2

The test substance was applied as received and the application sites were semi-occluded for the 4 and 1 hour exposure. The 3 minute site was left uncuffed during the exposure period.

B. Test Substance

The test substance, identified as methacrylic acid (Lot No. 6/4/96, assigned Rohm and Haas Toxicology Department Sample No. 96-054), was a clear liquid containing 99.38% active ingredient.

C. Animals and Animal Husbandry

Adult male New Zealand White rabbits were obtained from Hazleton Research Animals, Denver, PA. Upon arrival, all animals were examined for physical abnormalities, identified by uniquely numbered ear tags, and quarantined for approximately two weeks. The animals were individually housed in stainless steel cages (18x24x14.5 in., i.e. 46x61x37 cm) suspended above absorbent-paper pan liners which were changed 3 times per week. Throughout the test period, all rabbits had free access to filtered tap water (via automatic watering) and were fed

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132A

C. Animals and Animal Husbandry (Cont'd)

approximately 125 g/day of PMI Certified High Fiber Rabbit Diet 5325 (Purina Mills Inc., Richmond, IN). All animal rooms were environmentally controlled with controls set to maintain a temperature of approximately 65°F (18°C) and a relative humidity range of 30-70%. The temperature and relative humidity were monitored 24 hrs a day. During the study, the average daily temperature ranged from 64 to 66°F (18 to 19°C) and average daily humidity ranged from 54 to 68%. Excursions beyond these ranges were minimal and did not affect the integrity of the study. Temperature and humidity remained in compliance with acceptable ranges defined in the "Guide for the Care and Use of Laboratory Animals" NIH Publication No. 86-23, Revised 1996. The light cycle was automatically controlled, 12 hrs on and 12 hrs off.

One day prior to dosing, rabbits were selected from a healthy stock population. At the time they were dosed, the animals were approximately 19 to 30 weeks old and their body weights ranged from 2733 to 3484 g.

D. Dose Preparation and Administration

Approximately 24 hrs prior to the application of the test substance, the hair around the entire trunk between the flank and shoulders was shaved closely with electric clippers. The undiluted test substance (0.5 ml) was applied onto a 1.0-in. square gauze-lined adhesive bandage which was applied to the shaved intact skin of one rabbit for 4 hrs. A semi-occluded dressing (i.e., fabric cuff secured with adhesive tape) was used to wrap the entire trunk of the animal. The rabbit was returned to its cage for a 4 hr exposure period. An additional rabbit was tested on two separate sites for a 1 hr (right side) and 3 minute (left side) exposure. The 1 hr site was treated in the same manner as the 4 hr. The animal remained uncuffed during the 3 minute exposure. The cuff and patch were removed after the appropriate exposure and the application site wiped with paper towels saturated with tap water. The application site was blotted dry with paper towels. Two additional rabbits were tested for either a 1 hr or 3 minute exposure in the same manner as described above except these rabbits were washed with a 1% Ivory® soap solution prior to the tap water rinse.

E. Observations and Determinations

Skin irritation was evaluated at approximately 1, 24, 48, 72 hrs and at 7 and/or 14 days after patch removal. The degree of irritation was evaluated according to the

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132A

E. Observations and Determinations (Cont'd)

criteria of Draize et al. (J. Pharmacol. Exp. Therap. 82, 377-390, 1944), which are summarized in Appendix A. DOT Packing Group Classification guidelines are shown in Appendix B. In addition, all other skin reactions or signs of systemic toxicity were recorded. Animals were observed daily for mortality and reaction to treatment.

F. Location of Raw Data

All raw data, supporting documents, and records are stored in the Archives of the Toxicology Department, Rohm and Haas Company, 727 Norristown Road, P. O. Box 904, Spring House, PA 19477-0904.

III. RESULTS

Individual skin irritation scores (Draize criteria) are presented in Tables 1, 2 and 3. No mortality or clinical signs of systemic toxicity (other than skin effects) were observed during the study.

On all sites (4 hr, 1 hr and 3 minute), skin irritation indicative of corrosivity (i.e., concave eschar) was observed. On the 4 hr exposure site, severe erythema and very slight to severe edema was evident at all observation periods (1 of 1 rabbit). On the 1 hr site, severe erythema and very slight to moderate edema was observed at all observation periods (2 of 2 rabbits). One of these rabbits was euthanized after 24 hr scores due to the severity of the damage to the dermis (the subcutaneous muscle layer was visible and reddened). On the 3 minute site, severe erythema and very slight to moderate edema was evident at all observation periods (2 of 2 rabbits). One of these rabbits was euthanized after day 7 scores when conclusive evidence of irreversible damage (i.e. concave eschar, erosion and ulceration) was noted.

Washing the sites (1 hr or 3 minute) with a 1% soap solution did not affect the outcome of the study (corrosive effects were evident in animals receiving either the tap water rinse or the soap and water rinse).

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132A

IV. CONCLUSIONS

According to the Rohm and Haas Company Acute Toxicity and Irritation Hazard Categories (September, 1994), methacrylic acid is categorized as **CORROSIVE** to skin following a 4 hr exposure period (i.e., evidence of irreversible destruction of dermal tissue).

According to United Nations (U.N.) and U.S. DOT Packing Group Classification guidelines for Class 8 materials (1993 and 1996, respectively), methacrylic acid is assigned to **PACKING GROUP II** (i.e., full thickness destruction at the site of contact on the intact skin of rabbits within 14 days after an exposure time of more than 3 minutes, but not more than 60 minutes).

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132A

Table 1. Skin Irritation Scores (Draize Criteria)† - 4 Hr

ERYTHEMA:		Time After Patch Removal											
<u>Animal No.</u>	<u>1 hr</u>		<u>24 hrs</u>		<u>48 hrs</u>		<u>72 hrs</u>		<u>7 days</u>		<u>14 days</u>		
96-27222	4	ab	4	abc	4	abc	4	abc	4	abcd	4	acd	

EDEMA:	
<u>Animal No.</u>	
96-27222	4 3 2 1 1 1

† Scoring criteria is presented in Appendix A.

- a. Blackened
- b. Test substance adhered
- c. Application site perimeter: reddened
- d. Concave eschar

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132A

Table 2. Skin Irritation Scores (Draize Criteria)† - 1 Hr

ERYTHEMA:		Time After Patch Removal											
		1 hr		24 hrs		48 hrs		72 hrs		7 days		14 days	
<u>Animal No.</u>		4	ef	4	ef	4	ef	4	ef	4	def	4	def
96-27199		4	ef	4	ef	4	ef	4	ef	4	def	4	def
96-27242		4	a	4	g	-		-		-		-	
EDEMA:													
		<u>Animal No.</u>											
		96-27199	3	3		2		2		1		1	
		96-27242	3	3		-		-		-		-	

† Scoring criteria is presented in Appendix A.

a. Skin pulled off at time of patch removal

d. Concave eschar

e. Application site perimeter: reddened

f. Application site perimeter: blanching

g. All layers of dermis destroyed. Subcutaneous muscle layer visible and reddened.

(-) No applicable data. Animal was euthanized after 24 hr scores due to the severity of the damage to the dermis.

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132A

Table 3. Skin Irritation Scores (Draize Criteria)† - 3 Minute

ERYTHEMA:		Time After Patch Removal					
<u>Animal No.</u>	<u>1 hr</u>	<u>24 hrs</u>	<u>48 hrs</u>	<u>72 hrs</u>	<u>7 days</u>	<u>14 days</u>	
96-27199	4 e	4 ef	4 ef	4 ef	4 def	4 def	
96-27243	4 f	4 cf	4 cd	4 cd	4 cd	-	

EDEMA:							
<u>Animal No.</u>							
96-27199	3	3	2	2	1	1	
96-27243	3	3	2	1	1	-	

† Scoring criteria is presented in Appendix A.

c. Blackened

d. Concave eschar

e. Application site perimeter: reddened

f. Application site perimeter: blanching

(-) No applicable data. Animal was euthanized after Day 7 scores when conclusive evidence of irreversible damage to the dermis was noted.

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132A

Appendix A. Skin Irritation Scoring (Draize Criteria)

Erythema Scores (Maximum = 4)

No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema.....	2
Moderate to severe erythema.....	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4

Edema Scores (Maximum = 4)

No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well-defined by definite raising).....	2
Moderate edema (area raised approximately 1 mm).....	3
Severe edema (raised more than 1 mm and extending beyond area of exposure).....	4

Skin irritation is categorized on the basis of the Primary Irritation Index (PII). The PII is the sum of the erythema and edema scores at 1, 24, 48 and 72 hr divided by the number of observations (4), then divided by the number of animals (6).

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132A

Appendix B. United Nations¹ and United States² Department of Transportation Packing Group Classification Criteria

<i>Packing Group</i>	<i>Classification Criteria</i>
I	Full thickness destruction on intact skin tissue within an observation period up to 60 minutes starting after an exposure time of 3 minutes or less.
II	Full thickness destruction on intact skin tissue within an observation period up to 14 days starting after an exposure time of more than 3 minutes, but not more than 60 minutes.
III	Full thickness destruction on intact skin tissue within an observation period up to 14 days starting after an exposure time of more than 60 minutes, but not more than 4 hours.

¹U.N. Department of Transportation , United Nations Recommendations-Transport of Dangerous Goods, Chapter 8, Special Recommendations Relating to Class 8, 8th Edition, (1993).

²U.S. Department of Transportation , Class 8 - Assignment of Packing Group, 49 CFR, Section 173.137 (October 1, 1996).

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132A

Appendix C. Changes to the Original Report (96R-132)

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132

REPORT AMENDMENT NO. 1

Toxicology Department, Rohm and Haas Company
Spring House, PA

Test Compound: Methacrylic Acid

Type of Study: Skin Irritation Study in Rabbits

Report No.: 96R-132

Date of Amendment: 4/01/97

Report Sections Modified: Abstract, p. 6
Table of Contents, p. 7
Conclusion, p. 11
Appendix B, p. 16

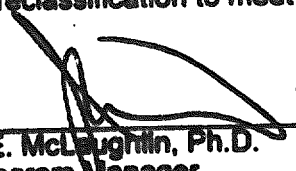
Changes to Report:

- p. 6 - The classification of MAA was changed to comply with current UN and US DOT Packing Group Classification.
- p. 7 - Changed Appendix title.
- p. 11 - The classification of MAA was changed to comply with current UN and US DOT Packing Group Classification.
- p. 16 - Changed the classification criteria to current UN and US DOT Packing Group Classification criteria. Changed references.


Reason for Changes: Business team requested reclassification to meet current UN and US DOT classification criteria.



J.R. Parno, M.S. Date
Study Director
Rohm and Haas Company



J.E. McLaughlin, Ph.D. Date
Program Manager
Rohm and Haas Company



B.A. Decker, B.S., Analyst, Date
Quality Assurance Unit
Rohm and Haas Company

Page 1 of 1